SUPPLEMENTAL MATERIAL

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Disclosures

Vivek Reddy's disclosures with medical companies (unrelated to this manuscript) include: Abbott (Consultant), Acutus Medical (Consultant, Equity), Affera (Consultant, Equity), Apama Medical (Consultant, Equity), Aquaheart (Consultant, Equity), Autonomix (Consultant, Equity), Axon (Consultant), Backbeat (Consultant, Equity), BioSig (Consultant, Equity), Biotronik (Consultant), Cardiofocus (Consultant), Cardionomic (Consultant), CardioNXT / AFTx (Consultant), Circa Scientific (Consultant, Equity), Corvia Medical (Consultant, Equity), Dinova (Consultant, Equity), East End Medical (Consultant, Equity), EBR (Consultant), EPD (Consultant, Equity), Epix Therapeutics (Consultant, Equity), EpiEP (Consultant, Equity), Eximo (Consultant, Equity), Impulse Dynamics (Consultant), Javelin (Consultant, Equity), Keystone Heart (Consultant, Equity), LuxCath (Consultant, Equity), Manual Surgical Sciences (Equity), Medlumics (Consultant, Equity), Medtronic (Consultant), Middlepeak (Consultant, Equity), Newpace (Equity), Nuvera (Consultant, Equity), Philips (Consultant), Stimda (Consultant), Surecor (Equity), Thermedical (Consultant), Valcare (Consultant, Equity), Vizara (Equity) and VytronUS (Consultant, Equity).

Jacob Koruth's disclosures with other medical companies include: Consultant – Medtronic, Vytronus, Abbott and Cardiofocus; Grant Support - Vytronus, Cardiofocus, Luxcath, Affera, LuxCath and Medlumics.

Study Definition Details

- Acute respiratory distress syndrome was defined by moderate to severe hypoxemia, PaO_2:FiO_2 < 200 (ratio of partial pressure of arterial oxygenation to fractionated inspired oxygenation) and bilateral pulmonary infiltrates on chest imaging unexplained by heart failure.
- Acute kidney injury was identified by a rise in serum creatinine of ≥ 0.3 mg/dl within 48 hours; or ≥1.5 times the baseline value within 7 days.
- Septic shock was defined according to the 3rd international consensus definitions for sepsis and septic shock guidelines.

Statistical Considerations

Covid-19 patients with cardiac injury (defined by elevated Troponin levels) have a higher incidence of adverse outcomes, including requiring mechanical ventilation and death. Covid-19 patients have reportedly high rates of cardiac arrhythmias (though poorly defined in most studies), ranging from 16.7% to 30.3%, with the highest rates being reported in critically ill patients, ranging from 44.4% to 74.6% (Wang et al). Accordingly, we hypothesized that Covid-19 patients that die will have a substantially higher incidence of acute malignant cardiac arrhythmias (AMCAs = VT/VF or AV block) than Covid-19 patients that survive to discharge.

For the power calculation, the incidence of AMCAs in the Mortality group is estimated to be 17%, based on Guo et al who reported a 17.3% rate of "malignant arrhythmia" (defined as >30 sec VT or VF) in patients with abnormal Troponin levels. Similarly, they reported a 1.5% rate of "malignant arrhythmia" in patients with normal troponin levels; accordingly, the estimated incidence of AMCAs in the discharged group is 3%.

In this retrospective/prospective study, consecutive patients were enrolled. We did not know what the relative rate of accrual between the two groups would be. Thus, if we required an equal number of patients between groups, we were concerned that a strategy of enrolling that target number in one group and thereafter only accumulating patients in the other group, might introduce a bias in enrollment as treatment strategies varied over time. Accordingly, the below sample size curve was constructed to determine the requisite sample size, yet accommodating a number of potential Discharged:Mortality accrual ratios. The below power calculations are based on an 80% chance of detecting, as significant at the 5% level, an increase in the primary outcome from 3% in the Discharged group to 17% in the Mortality group. For example, a sufficient sample size would be 46 patients in the Mortality group, and 101 in the Discharged group.

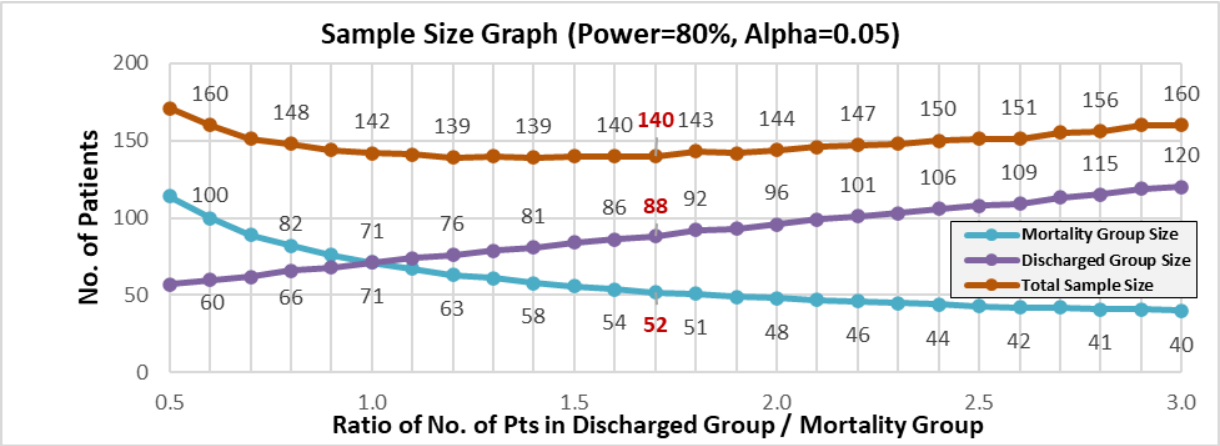


Table S1: Telemetry *vs* No Telemetry Patients that Died: Selected Demographics, Clinical and Laboratory Data & Outcomes

Characteristics	Death – Telemetry (N = 52)		Death – No Telemetry (n = 78)		p-value
	No. with Available Data	Value	No. with Available Data	Value	
Median age (IQR) – year	52	71 (58 – 78)	78	76 (63-87)	**0.03**
Male gender (%)	52	38 (73)	78	39 (50)	**0.01**
Body mass-index, median (IQR)	52	29.7 (26.7 – 35.2)	75	27.5 (23.9-32.5)	**0.03**
Comorbidities – no. (%)					
Obesity (Body mass-index ≥30)	52	25 (48)	75	30 (38)	0.30
Chronic kidney disease	52	13 (25)	78	17 (22)	0.67
Chronic dialysis	52	4 (8)	78	10 (13)	0.40
Laboratory Data – On Admission *					
D-dimer					
On admission, μg/mL	45	2.4 (1.0 – 4.2)	72	2.5 (1.4-6.0)	0.50
Troponin-I					
On admission, ng/mL	49	0.03 (0.01 – 0.21)	75	0.04 (0.02-0.2)	0.70
Peak level, ng/mL	47	0.27 (0.06 – 2.1)	64	0.08 (0.03-0.39)	**0.02**
C-reactive protein, mg/L	49	146 (61 – 219)	72	163 (103-232)	0.23
Complications					
Myocardial injury – no. (%)	52	39 (75)	63	47(60)	0.09
Palliative Care – no. (%)	52	20 (38)	78	38 (49)	0.30
Composite Primary Outcomes					
Total – no. (%)	52	9 (17)	78	1 (1)	**0.01**†
Ventricular Tachycardia or Fibrillation – no. (%)	52	6 (12)	78	1 (1)	**0.02**
Atrioventricular block – no. (%)	52	3 (6)	78	0 (0)	0.06
Secondary Outcome					
Acute myocardial infarction – no. (%)	52	4 (8)	78	2 (3)	0.22

All values are expressed as median (IQR), unless otherwise specified.
* Values are upon admission, unless otherwise specified.
† Poisson Regression Analysis shows a HR 13.6, 95% CI (1.7 - 107.9), p=0.01

Table S2: Descriptive Analysis of Acute Malignant Cardiac Events, and Relationship to Death

Patient No.	Event	Comfort Care?	Outcome	Brief Description	Clinical interpretation as to whether this acute cardiac event was a primary causative factor in death?	
					Y/N	Rationale
Mortality Group						
1	MI & AVB	N	Death	77 yo, ARDS, renal failure, shock, ST elevation noted on telemetry prior to AVB and then arrest.	Y	
2	MI	Y	Death	92 yo, hypoxemic respiratory failure, new LBBB with elevated troponin (206), PEA arrest.	Y	
3	AVB	Y	Death	61 yo, ESRD, shock, hyperkalemia (8.0), care withdrawn, AVB.	N	Hyperkalemic (8.0), Severe ARDS (P:F 85)
6	VT/VF	N	Death	55 yo, CABG, acute MI with VF arrest leading to VA ECMO prior to becoming COVID+ on hospital day 20. Hypoxic PEA arrest.	N	VT/VF event occurred prior to COVID infection
7	VT/VF	N	Death	50 yo, pulmonary sarcoidosis, renal failure, refractory metabolic and respiratory acidosis, VF arrest.	N	Acidosis (pH 7.05), Hyperkalemia (6.3)
8	VT/VF	N	Death	64 yo, DM2, DKA with acidosis and hyperkalemia with PMVT/VF arrest.	N	Hyperkalemia (7.4), Autopsy—pulmonary embolism
9	AVB	N	Death	58 yo, renal failure, shock, new RBBB with progressive AVB leading to arrest.	N	Shock (2 high dose vasopressors)
11	VT/VF	Y	Death	74 yo, HTN, progressive hypoxia leading to VF arrest.	N	Hypoxia (Spo2 66%)
12	MI	N	Death	64 yo, renal failure, ARDS, inferolateral STEMI, elevated troponin (21) with refractory shock leading to PEA arrest.	Y	
13	VT/VF	N	Death	68 yo, metastatic lung cancer, seizures and neutropenic fever. VF arrest during intubation.	N	Hypoxia (Spo2 80%)
14	VT/VF	Y	Death	48 yo, HIV, ARDS, refractory shock leading to VF arrest.	N	Severe ARDS (P:F 63), Shock (2 high dose vasopressors), Autopsy—pulmonary embolism.
16	MI	Y	Death	81 yo, dementia, ST elevations in leads V2-V6, elevated troponin (12.6) and newly depressed EF (36%) (**No. 5; Table S5**)	Y	
Discharged Group						
4	MI	N	Discharged	78 yo, HTN, presenting with shortness of breath with ST elevations in leads I, II, V2-V6 with elevated troponin (11).		
5	VT	N	Discharged	88 yo, NICM (EF 35%) presenting with chest pain and pneumothorax, MMVT.		
10	AVB & MI	N	Discharged	84 yo, ST elevations in leads II, III, aVF, 2:1 CHB with widening QRS, TVP placed and conduction recovered.		
15	AVB	N	Discharged	65 yo, w/ CHB elevated troponin (10.2), EF 32% with subacute lesion on angiography, required a pacemaker. (**No. 4; Table S5**)		

Table S3: Descriptive Analysis of Patients with AV block

Pt No. (based on Table S2)	Age (yrs)	Gender	Baseline QRS duration	Intubation	Time course of AV block (days)	Escape rhythm	TVP	PPM	Outcomes	Arrhythmia at time of death	Pertinent clinical history
1	77	Male	Narrow	Yes	6	No escape	No	No	Death	PEA	Inferior-lateral ST-elevation
3	61	Male	Narrow	Yes	1	Wide escape	No	No	Death	PEA	Hx ESRD w/hyperkalemia (K^+=8 meq/L).
9	58	Male	Narrow	Yes	8	Wide (LBBB)	No	No	Death	PEA	Shock (2 high dose vasopressors)
10	84	Male	IVCD	No	4	Wide (LBBB)	Yes	No	Discharged	-	Inferior STEMI
15	65	Female	Narrow	No	1	Wide (LBBB)	Yes	Yes	Discharged	-	NSTEMI. Coronary angiogram showed diffuse disease, no intervention was performed.

TVP: Transvenous pacemaker; PPM: Permanent pacemaker; ESRD: End stage renal disease; IVCD: Intraventricular conduction delay; PEA: Pulseless electrical activity

Table S4: Predictors of Mortality – Univariable Analysis

Factor	Death (N=52)	Survived (N=88)	P-value
Age>65 yes, N (%)	30 (58)	29 (33)	**0.005**
Coronary artery disease, N (%)	13 (25)	22 (25)	1.0
Hypertension, N (%)	35 (67)	51 (58)	0.3
Obesity, N (%)	25 (48)	27 (31)	**0.05**
Admission creatinine >1.5 mg/dl, N (%)	16 (31)	17 (19)	0.1
Myocardial injury †, N (%)	23 (44)	21 (24)	**0.01**
Admission D-dimer>1 µg/m, L, N (%)	34 (65)	45 (51)	0.1
Admission IL-6>100 pg/Ml, N (%)	26 (50)	21 (24)	**0.003**
Vasopressor during hospitalization, N (%)	36 (71)	10 (12)	**<0.0001**
ARDS, N (%)	34 (66)	8 (9)	**<0.0001**
Composite Primary Outcomes, N (%)	9 (17)	3 (3)	**0.009**

† Based on peak Troponin I value.

Table S5: Predictors of Mortality – Multivariable Binary Logistic Regression Analysis *

Factor	Hazard Ratio (95% CI)	p-value
Age>65 yes	3.10 (1.10-9.37)	**0.05**
Obesity	1.11 (0.38-3.30)	0.84
Myocardial injury †	2.26 (0.72-7.10)	0.16
Admission IL-6>100 pg/mL	1.27 (0.40-4.10)	0.68
Vasopressor during hospitalization	4.97 (1.44-17.10)	**0.01**
ARDS	12.93 (3.20-52.17)	**<0.0001**

* Mutltivariable binary logistic regression analysis was performed to calculate the odds ratio to estimate the association of risk between mortality and various covariates. The dependent variable in the model was mortality. Those variables which were significant on univariable analysis and had ≥10 events were included in the multivariable model. All covariates were considered as categorical variables.

† Based on peak Troponin I value.

Table S6: 12-Lead Electrocardiographic and Telemetric Monitoring

Characteristics	All Patients (N=140)	Death (N=52)	Survived (N=88)	p-value
Baseline Electrocardiogram				
Heart rate/min, median (IQR)	88 (75 – 103)	88 (76 – 107)	88 (73 – 102)	0.6
Rhythm				
Normal sinus rhythm – no. (%)	98 (70)	30 (58)	68 (77)	**0.02**
Sinus tachycardia – no. (%)	18 (13)	10 (19)	8 (9)	0.1
Atrial fibrillation – no. (%)	14 (10)	9 (17)	5 (6)	**0.04**
Other – no. (%)	10 (10)	3 (6)	7 (8)	0.7
Duration of PR interval – msec	150 (135 – 168)	152 (134 – 196)	147 (137 – 166)	0.4
Duration of QRS interval – msec	88 (80 – 100)	90 (77 – 110)	86 (80 – 98)	0.3
Duration of QT_C interval – msec	443 (425 – 470)	444 (425 – 486)	442 (425 – 464)	0.3
Right bundle branch block – no. (%)	11 (8)	6 (11)	5 (6)	0.3
Left bundle branch block – no. (%)	1 (1)	1 (2)	0	0.4
Intraventricular conduction delay – no. (%)	9 (6)	5 (10)	4 (4.5)	0.3
Presence of ST-T changes – no. (%)	53 (38)	22 (42)	31 (35)	0.4
Last Electrocardiogram prior to death or hospital discharge				
Rhythm				
Normal sinus rhythm – no. (%)	88 (63)	31 (60)	57 (65)	0.6
Sinus tachycardia – no. (%)	34 (24)	13 (25)	21 (24)	1.0
Atrial fibrillation – no. (%)	11 (8)	5 (10)	6 (7)	0.6
Other – no. (%)	7 (5)	3 (6)	4 (5)	0.1
Duration of QT_C interval – msec	450 (432 – 477)	458 (417 – 490)	449 (433 – 473)	0.5
No. with QTc increase by ≥ 50 msec – a no. (%)	13 (9)	7 (13)	6 (7)	0.20
Presence of new ST-T changes – no. (%)				
ST-elevation – no. (%)	2 (1)	0 (0)	2 (2)	0.5
ST-depression – no. (%)	7 (5)	1 (2)	6 (7)	0.4
T-wave inversion – no. (%)	15 (4)	7 (13)	8 (9)	0.4
Markers of new right ventricular strain				

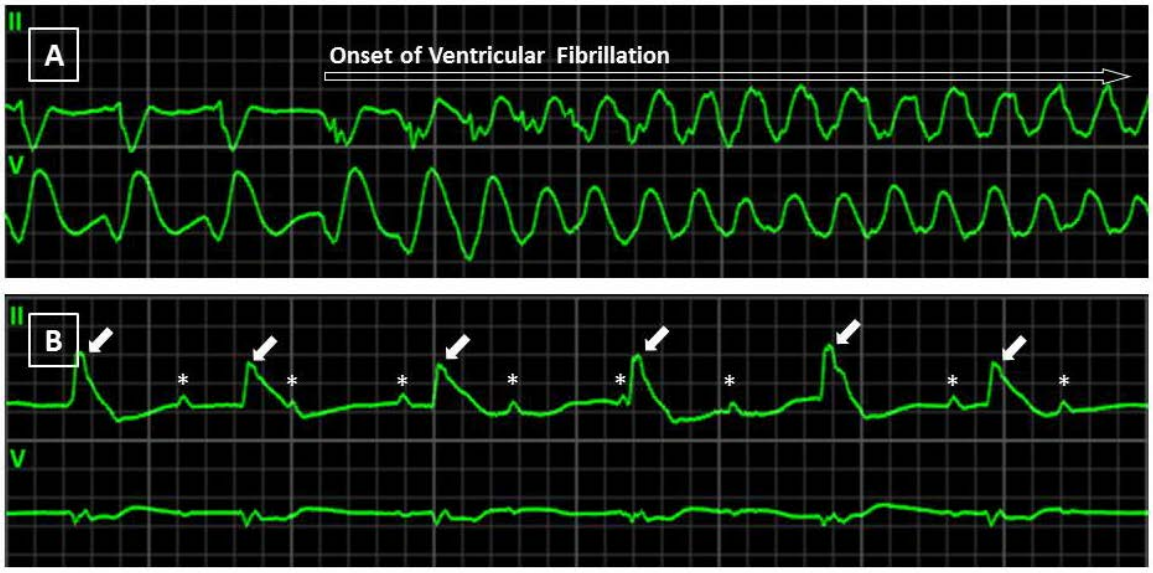
Right axis deviation – no. (%)	3 (2)	2 (4)	1 (1)	0.5
Right Bundle Branch Block – no. (%)	2 (1)	1 (2)	1 (1)	1.0
ST-T changes in leads V1-V4 – no. (%)	3 (2)	0	3 (3)	0.3
ST-T changes in inferior leads – no. (%)	8 (6)	5 (10)	3 (3)	0.15
Met >1 criterion for $S_1Q_3T_3$ – no. (%)	3 (2)	0	3 (3)	0.3
Telemetry				
Duration of continuous monitoring, hours	120 (72 – 168)	120(72 – 192)	120 (48– 168)	0.32
Atrial arrhythmias – no. (%)				
Atrial fibrillation or flutter – no. (%)	28 (20)	18 (35)	10 (11)	**0.002**
Atrial fibrillation – no. (%)	24 (17)	15 (28)	9 (11)	**0.009**
Atrial flutter – no (%)	6 (4)	5 (10)	1 (1)	**0.03**
Atrial tachycardia – no. (%)	40 (28)	18 (35)	22 (25)	0.24
Supraventricular tachycardia – no. (%)	4 (3)	3 (6)	1 (1)	0.10
Ventricular arrhythmias – no. (%)				
Monomorphic Ventricular tachycardia – no. (%)	1 (1)	0 (0)	1 (1)	1.00
Ventricular fibrillation – no. (%)	6 (4)	6 (11)	0 (0)	**0.01**
Premature ventricular contractions (PVC) – no. (%)				
Occasional isolated PVCs– no. (%)	23 (16)	11 (21)	12 (14)	0.24
PVCs >1/min – no. (%)	14 (10)	4 (8)	10 (11)	0.60
Multiform PVCs – no. (%)	4 (3)	1 (2)	3 (3)	1.00
Couplets – no. (%)	3 (2)	2 (4)	1 (1)	0.55
Non-sustained ventricular tachycardia – no. (%)	9 (6)	5 (10)	4 (4.5)	0.30
Bradyarrhythmias – no. (%)				
Atrioventricular Block – no. (%)	5 (3.5)	3 (6)	2 (2)	1.00
Pulseless Electrical Activity – no. (%)	46 (33)	46 (88)	0 (0)	**<0.0001**

All values are expressed as median (IQR), unless otherwise specified.

Table S7: Descriptive Analysis of Available Echocardiographic Imaging

Patient No.	Outcome	Indication for Echocardiogram	Echocardiogram Findings
1	Discharged	49 yo, prior CVA p/w aphasia with acute stroke on CTA s/p thrombectomy.	Normal biventricular size and function, no valvular pathology or intracardiac mass. No intracardiac shunting with agitated saline.
2	Death	67 yo, lung cancer with worsening shock and pericardial effusion on POCUS. TTE performed during pericardiocentesis.	Confirmed presence of effusion. Normal left ventricular size and function.
3	Discharged	46 yo, shortness of breath with persistent sinus tachycardia.	Normal Biventricular size and function.
4	Discharged	65 yo, w/ CHB elevated troponin (10.2), EKG absent clear ischemic changes **(No. 15 on Table S2).**	EF 32% with hypocontractile septum inferior and apical walls.
5	Death	81 yo, dementia, ST elevations in leads V2-V6, elevated troponin (12.6) **(No. 4 on Table S2).**	Newly depressed EF 36%, hypocontractile apex and anteroseptal walls.
6	Death	59 yo, Afib on Xarelto with progressive dyspnea and lower extremity edema. Suffered PEA arrest.	Normal biventricular size and function, no valvular abnormalities.
7	Discharged	26 yo, elevated transaminases.	Normal biventricular size and function, no valvular abnormalities.
8	Discharged	37 yo, aphasia and right sided weakness, CTA with distal acute stroke.	Normal biventricular size and function, agitated saline study demonstrating early left sided bubbles.
9	Death	72 yo, with elevated troponin (10.3), borderline EKG changes.	Normal biventricular size and function. No segmental wall motion abnormalities

<u>Figure S1</u>: Cardiac Arrhythmias. Shown are example of the onset of ventricular fibrillation (**A**) and atrio-ventricular block in the setting of an acute myocardial infarction (**B**). For the latter, the p waves are indicated by the asterisks, and the arrows denote the QRS complexes with ST elevation.



References

1) Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323:1061-1069.
2) Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol*. 2020;e201017. doi: 10.1001/jamacardio.2020.1017